UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,982	03/28/2005	Akira Kakizuka	2005_0199A	1176

513 7590 06/09/2008

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
06/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,982	KAKIZUKA ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments filed March 5, 2008 have been received and entered. Applicants have cancelled claims 1-3, while claims 4-9 have been added.

Election/Restrictions

Applicant's election of claims 1-2 (group I) in the reply filed on June 20, 2006 was acknowledged. Applicants' have also elected cells obtained from established human or non-human cell line; that is adipocyte cells; and BAT as species for examination in the reply filed March 5, 2008.

Claims 4-9 are under consideration.

Information Disclosure Statement

The reference JP 2002-58489 (AK in IDS) is considered to the extent it is presented in English. It is noted that only abstract has been considered, while rest of the disclosure that is in not in English language has not been considered.

Withdrawn-Claim Rejections - 35 USC § 112

Claim 2 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of cancellation of the claims.

Withdrawn -Claim Rejections - 35 USC § 112

Claims 1-2 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is withdrawn in view of cancellation of the claims.

Claims 1-2 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of cancellation of claims 1-2.

New-Claim Rejections-Necessitated by amendments - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Instant claim 7 (c) recites identifying the candidate compounds increasing the activity for expressing the MCAD gene to the level of same as action of ERRL1 to ERR, however, none of the earlier method step set forth any step involved in method/process to measure action of ERRL1 to ERR, it is unclear what method /process applicant is intending to encompass for 7 (c) for comparison purposes. The term "as same as the action of ERRL1 for ERR" does not further clarify the comparative step with respect to MCAD gene. Recitation of additional method to address this issue would obviate the basis of this rejection. Claim 8-9 depends on claim 7 and therefore are included in the rejection. Appropriate correction is required.

Withdrawn- Claim Rejections - 35 USC § 102

Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Spiegelman et al (US Patent publication no. 2003/0124598, dated 7/3/2003, effective filing date 11/09/2001, IDS) is withdrawn in view of newly submitted claims that require specific method steps not taught by Spiegelman et al .

Claims 1-2 rejected under 35 U.S.C. 102(b) as being anticipated by Spiegelman et al (WO00/32215, dated 06/08/2000, IDS) is withdrawn for the reasons set forth above.

Claim 2 rejected under 35 U.S.C. 102(b) as being anticipated by Scheen et al (Diabetes Metab Res Rev. 2000; 16(2):114-24) is withdrawn in view of cancellation of the claims.

New-Claim Rejections-Necessitated by amendments - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiegelman et al (US Patent publication no. 2003/0124598, dated 7/3/2003, effective filing date 11/09/2001, IDS) and Huss et al (The Journal of Biological Chemistry 277, 43, 40265-40274) or Hentschke et al (Biochemical and Biophysical Research Communications, 2002, 299, 872–879).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

It is noted that applicants have presented new claims that have includes additional method steps that require contacting cells expressing ERRL1 and ERR with a candidate agent, measuring the binding and then identifying the candidate that promote binding of ERRL1 to ERR. Additionally, claims have been amended to

read on specific cell in which ERRL1 protein is highly expressed, a limitation that was not required by earlier claims and therefore a new rejection is proper.

Spiegelman et al teach an isolated nucleic acid molecule PGC-1beta, which encode novel PGC-1 related co-activator molecules (abstract). It is noted that the isolated nucleic acid molecule disclosed by Spiegelman may comprise a nucleotide sequence, which is at least about 50- 99.99% or more identical to the entire length of the nucleotide sequence (page 2 and 3, paragraph 20). The specification discloses ERRL1 sequence after searching expression sequence tags for PGC-1 related molecule. It is noted that that PGC-1 homologue named PGC-1β has only one amino acid difference from ERRL1 (see page 26 lines 11-22 of the specification). Therefore, the nucleic acid sequence disclosed by Spiegelman with 99.9% or more homology of PGC-1 beta would meet the claim limitation of ERRL1. It is emphasized that Spiegelman reference is applied to the extent it teaches nucleotide sequence of ERRL1. Spiegelman teach contacting a cell which expresses a PGC-1b(ERRL1) with a test compound to determine the ability of the test compound to interact and/or co activate with a nuclear receptor (see para. 193 of the specification). Spiegelman also discloses a method of screening drug that has an ability to modulate PGC-1b binding to a target molecule (a nuclear receptor or HCF) by coupling the PGC-1b (ERRL), target molecule with a radioisotope or enzymatic label such that binding of the PGC-1b (ERRL) target molecule to PGC-1b (ERRL1) could be determined (see para. 192-193 of the specification). Furthermore, Spiegelman et al also disclose screening assay in cells of mammalian origin including brown adipose cell derived from brown adipose tissue such as a HIB1B cell, a heart cell, or a liver cell meeting the limitation of claims 5-6, 8-9 (see para. 55 and 193). Although, Spiegelman teaches contacting cells expressing ERRL1 with candidate compound and then measuring the binding of ERRL1 with other nuclear receptor in mammalian brown adipose tissue cells to identify agent that modulates the binding or interaction of

PGC-1beta with nuclear receptor, but differed from claimed invention by not explicitly teaching the nuclear receptor being ERR.

Huss et al cured the deficiency of Spiegelman et al by reporting a two-hybrid screen of an adult human heart cDNA library in yeast using PGC-1 as bait to show orphan nuclear receptor, estrogen-related receptor (ERR alpha) as a novel PGC-1 interacting protein. PGC-1 alpha enhanced the transcriptional activities of ERR alpha and the related isoform ERR alpha. Huss also teaches that the PGC-1alpha-ERR alpha complex directly activate the MCAD promoter that was previously shows as an ERR alpha target (see page 40266, col.1, para. 4). Furthermore, it is noted that forced expression of ERR alpha in cardiac cells significantly induced the expression of MCAD (see page 40268, col.2, last para) meeting the limitation of claims 7-8 reciting cells expressing ERR and measuring the activity of ERR for expressing the MCAD gene (see Figure 2C). Huss teaches that binding of the ERR alpha isoform with PGC-1 alpha by measuring GST-PGC338 with 35S-labeled ERRalpha. (See figure 1B and 4B and figure 5). Like wise Henrschke et al disclose upon co transfection of both PGC-1 and PERC stimulate transcriptional activation by ERR ganna, while pull-down experiments reveal a direct interaction of ERRgamma with both coactivators. Specifically, Henrschke et al disclose co transfection of cells with reporter plasmid and either expression plasmids without insert, or coding for ERRgamma and PGC-1 (see Figure 2 and 3) indicating PGC-1 functions as an ERR gamma coactivator. Although, Huss/ Henrschke taught contacting cells that express PGC and ERR and measuring binding of ERRL1 to ERR but differed from claimed invention by not explicitly teaching screening compounds that promote the binding of ERRL1 to ERR.

Accordingly, in view of the teachings of Spiegelman et al, Huss/ Henrschke, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of screening compound disclosed by Spiegelman et al to substitute target molecule (nuclear receptor or HCF) with

functionally equivalent another nuclear receptor ERRα or ERRγ as taught by Huss/ Henrschke with a reasonable expectation of success. It would have been *prima facie* obvious to one of ordinary skill in the art to combine the references, as Spiegelman et al had already sought to screen compounds by a method comprising contacting cells that express PGC-1 (ERRL1) and target nuclear receptor and then measuring the binding of PGC-1 (ERRL1) to the nuclear receptor in order to identify the candidate compound (supra). Furthermore, Huss provided the guidance that PGC-1 acts as tissue specific co activators and forced expression of ERR increases the MCAD activity in the cells implicating ERR isoforms in the regulation of mitochondrial energy metabolism by suggesting a potential mechanism whereby PGC-1apha selectively binds transcription factor partners (see Huss, abstract). Therefore, given that orphan nuclear ERR was known to interact with PGC-1. It would have *prima facie* obvious for one of ordinary skill to modify the method disclosed by Spiegelman to substitute one known element with another (ERRa) with reasonable expectation of achieving predictable result in screening compounds. One who would practiced the invention would have had reasonable expectation of success because molecular cloning of sequences, co transfection and two hybrid system was standard technique at the time of filing of this application and Spiegelman et al, Huss/ Henrschke both sought to study the interaction of PGC-1 (EERL1) with the nuclear receptor for identifying compounds that promote such binding to compound that increases the activity of ERR for expressing MCAD.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiegelman et al (US Patent publication no. 2003/0124598, dated 7/3/2003, effective filing date 11/09/2001, IDS), Vega et al (Dissertation Abstracts International, (1999)

Vol 60, No. 9B, p. 4366)/ Vega et al (Mol Cell Biol. 2000 March; 20(5): 1868–1876) and Saldek et al (Molecular and Cellular Biology, 1997, 5400-5409).

The reference of Spiegelman has been discussed above and relied in same manner here. Although, Spiegelman teaches contacting cells expressing ERRL1 with candidate compound and then measuring the binding of ERRL1 with other nuclear receptor in mammalian brown adipose tissue cells to identify agent that modulates the binding or interaction of PGC-1beta with nuclear receptor, but differed from claimed invention by not explicitly teaching the nuclear receptor being ERR.

The deficiency of Spiegelman is cured by Vega who reported the transcriptional induction of nuclear gene encoding a key mitochondrial FAO enzyme (MCAD) gene during brown adipocyte differentiation required the pleiotropic nuclear receptor response element, NREE-1 (see abstract of dissertation and page 30-39). The orphan nuclear receptors COUP-TF and ERR alpha bind NREE-1 in brown adipocyte differentiation stage specific manner. Additionally, Vega identifies MCAD as potential ERR alpha target (see abstract and page 30 of dissertation). Vega et al also show that the co activator PGC-1 co operates with PPAR alpha in the transcriptional control of nuclear gene encoding mitochondrial fatty acid oxidation enzyme (MCAD) (see figure 2 of Vega MCB paper). However, Vega differed from claimed invention by not disclosing contacting cells with candidate agent to measure binding of PGC-1 with (ERRL1) to ERR.

Sladek et al teach ERR alpha is most highly expressed in kidney, heart, and brown adipocytes, tissues which binds to an ERRa response element (ERRE) containing a single consensus half-site, TNAAGGTCA. Sladek et al teach MCAD nuclear receptor response element 1 (NRRE-1) interacts in vitro with ERRa expressed in COS-7 cells and supershift assay shows that endogenous ERRalpha

present in nuclear extracts obtained from a brown fat tumor cell line (HIB) interacts with NRRE-1 (see figure 7).

Accordingly, in view of the teachings of Spiegelman et al, Vega and Saldek, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of screening compound disclosed by Spiegelman et al to substitute target molecule (nuclear receptor or HCF) with functionally equivalent another nuclear receptor ERR□ with a reasonable expectation of success. At the time of the invention, PGC-1 was known that induction of MCAD gene during brown adipocyte differentiation requires the pleiotropic nuclear receptor response element, NREE-1 and PGC-1 co operates with PPAR alpha in the transcriptional control of MCAD (see Vega). Given that one of ordinary skill in the art was aware that MCAD nuclear receptor response element 1 (NRRE-1) interacts in vitro with nuclear receptor ERRalpha. It would have been *prima facie* obvious to one of ordinary skill in the art to pursue the known options with his or her technical grasp to include ERR alpha as target molecule with reasonable expectation for the coactivation of ERR alpha by PGC-1. Spiegelman et al had already sought to screen compounds by a method comprising contacting cells that express PGC-1 (ERRL1) and target nuclear receptor and then measuring the binding of PGC-1 (ERRL1) to the nuclear receptor in order to identify the candidate compound (supra). Furthermore, Vega provided the guidance that forced expression of ERR increases the MCAD activity in the cells (see page 39 and abstract). Therefore, given that orphan nuclear ERR was known to interact with MCAD, while co-activator PGC-1 is also involved in the transcriptional control of MCAD. It would have *prima facie* obvious for one of ordinary skill to modify the method disclosed by Spiegelman to include ERRa as the target molecule with reasonable expectation of achieving predictable result in screening compounds. One who would practiced the invention would have had reasonable expectation of success because molecular cloning of sequences, co transfection and two hybrid system was standard technique

at the time of filing of this application and Spiegelman et al, Vega and Saldek sought to study the interaction of PGC-1 (EERL1) with the nuclear receptor by transcriptional regulation of MCAD.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No Claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ichida et al (J. Biol. Chem., Vol. 277, Issue 52, 50991-50995, December 27, 2002); Vega et al (Dissertation Abstracts International, (1999) Vol 60, No. 9B, p. 4366)

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh
AU 1632

/Thaian N. Ton/
Primary Examiner, Art Unit 1632